Reviewer's report

Title: Whole genome methylation array analysis reveals new aspects in Balkan Endemic Nephropathy etiology

Version: 5 Date: 9 June 2013

Reviewer: Ljubica Djukanovic

Reviewer's report:

Thank you for giving me opportunity to review the manuscript “Whole genome methylation array analysis reveals new aspects in Balkan Endemic Nephropathy etiology” by Rada G Staneva and co-workers. The authors investigated the methylation status across whole-genome in several groups of patients with Balkan endemic nephropathy (BEN) and healthy controls from non-endemic regions. Different methylated regions (DMRs) were determined in different patient control pairs. Hypomethylation of the promoters of genes HDAC11, IL-17RA, SECG61 was found in BEN patients as compared to controls.

These are the first data on whole genome DNA methylation array in BEN that add new insight into the understanding of the disease.

I have several comments.

Major Compulsory Revisions

Abstract. The results obtained do not lead to the conclusion expressed in the last sentence of abstract.

Background. Page 5, line 4-5 - The claim that the disease is more common in females than in males is not fully accurate. As authors state later in the text, both genders are similarly affected in Serbia. It is generally accepted that BEN affects both gender equally, even with slight female predominance.

Page 5, line 7. BEN is slow progressive chronic kidney disease but it is not true that the disease inevitably leads to ESRD. Some patients die in their eighties in the earlier stages of CKD.

Methods. The authors write “Clinical assessment was performed according to unified criteria.…” and also “Diagnosis of Balkan endemic nephropathy was set according to current diagnostic criteria.”. It is necessary to describe method of clinical assessment and diagnostic criteria or to cite the paper in which it is precisely described.

Page 9, line 1 - Definition of control group is incomplete. The first sentence on page 9 says: “Control samples were collected from non-endemic regions in Bulgaria and Serbia after exclusion of family history of kidney disease.” As authors say that control group consisted of 170 healthy individuals it is necessary to describe what was definition of healthy.
Discussion. It is generally agreed that the morphological changes of BEN correspond to non-destructive non-inflammatory kidney disease. The author mention “inflammatory changes in BEN” (page 14, line 10) and that should be corrected.

Minor Essential Revisions

Page 5, line 4 – instead Bosnia, Herzegovina should be Bosnia and Herzegovina.

Page 5, line 9 - after the word “tract” [4] should be deleted.

Typographical errors should be corrected.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.